

## Harnessing native fat-residing stem cells for bone regeneration

### Grant Award Details

Harnessing native fat-residing stem cells for bone regeneration

**Grant Type:** Early Translational II

**Grant Number:** TR2-01821

**Project Objective:** The goal of the project is to use purified adipose derived MSC stem cells for instance spine fusion

**Investigator:**

**Name:** Bruno Peault  
**Institution:** University of California, Los Angeles  
**Type:** PI

**Name:** Chia Soo  
**Institution:** University of California, Los Angeles  
**Type:** Co-PI

**Disease Focus:** Bone or Cartilage Disease

**Human Stem Cell Use:** Adult Stem Cell

**Cell Line Generation:** Other

**Award Value:** \$5,359,076

**Status:** Closed

### Progress Reports

**Reporting Period:** Year 1

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**Reporting Period:** Year 2

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**Reporting Period:** Year 3 +NCE

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## Grant Application Details

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**Application Title:** Harnessing native fat-residing stem cells for bone regeneration

**Public Abstract:** Like most tissues of the body, bone possesses a natural regenerative system aimed at restoring cells and tissues lost to natural cell aging, disease or injury. These natural regenerative systems are complex combinations of cell growth factors and support structures that guide and control the development of specialized bone stem cells. However, the regeneration process may still fail, for multiple reasons. For instance, the degree of skeletal injury may be so great that it overwhelms the natural regenerative capacity. Alternatively, the natural regenerative capacity may be defective; this is exemplified by osteoporosis, a frequent condition affecting post-menopausal females and elderly males and females. Osteoporotic individuals have severe declines in stem cell numbers (10-fold decrease from age 30 to 80) and stem cell function (tendency of stem cells to turn into fat rather than bone cells with age), leading to bone loss and "fragility fractures" that typically would not occur in persons with normal stem cell number and function. Thus, there is a tremendous need for therapies to increase the number and function of endogenous adult stem cells with the potential to build new bone.

One option is to introduce so called mesenchymal stem cells (MSC) from the patient to bone repair sites. However, significant hurdles to autologous MSC use include the need for 2-3 week culture times to isolate MSC before application. Moreover culturing introduces infectious and immunogenic risks from prolonged exposure to animal products and cancerous risks from cellular gene changes in culture. In addition, once isolated, MSC require appropriate growth factor stimulation to form bone. Finally, MSC isolated from patient tissues such as fat or bone marrow are heterogenous and of undetermined composition—making growth factor dosing and conformance with FDA regulations for defining target product identity, purity, and potency more difficult.

To circumvent these problems, we have identified and purified the cells at the origin of human MSC. We have termed these perivascular stem cells (PSC) because they are natively localized around all arteries and veins, forming the key cellular component of the natural regenerative system. In a significant breakthrough, we are able to isolate these cells within hours from adipose tissues in sufficient numbers for therapy without the need for culture. This realizes the possibility of harvesting and implanting stem cells during the same operative period. In another breakthrough, we have identified a potent growth factor NELL-1 that potently amplifies the ability of PSC to form bone and vascular structures. This has led to the development of our target PSC+NELL-1 product, which effectively stimulates and augments the body's natural bone regenerative system by providing all the components (stem cells, growth factor, and allograft bone support structure) necessary to "jump start" as well as maintain the function of bone stem cells.

**Statement of Benefit to California:**

This FDA oriented proposal focuses on crucial preparatory work required before IND-enabling preclinical studies on our Developmental Candidate for bone formation and regeneration. Our Developmental Candidate provides a complete package of stem cells, bone growth factors, and scaffold to build an optimized microenvironment to "jump start" bone formation in normal and impaired bone healing conditions. We have generated very promising preclinical data on our Developmental Candidate's superior bone formation and regeneration efficacy. In addition to its significant impact on health care, this highly multi-disciplinary project by our team has many near-term and long-term benefits to the State of California.

1. Besides direct health costs, musculoskeletal injuries and diseases are the leading cause of work-related and physical disability in the United States. Hard working Californians are responsible for California's annual gross domestic product of \$1.8 trillion, which rank our state among the top eight largest economies in the world. By promoting the repair of both normal and healing-impaired bone in a safe and effective manner, our mature technology will reduce the loss of work productivity at the front end, reduce work disability costs, and reduce the loss of state income tax.

2. Local osteogenic stem cells decline with age (from 1/10,000 in newborns to 1/250,000 by age 30 and 1/2,000,000 by age 80), leading to osteoporosis, poor bone quality, and fragility fractures. In 1998, the health care burden for osteoporosis exceeded \$2.4 billion in California alone. A whopping 64% of the \$2.4 billion was caused by hip fracture. If our Development Candidate is successful in healing existing fractures in impaired bone, it may also translate to therapies to prevent fractures in impaired bone. This will significantly reduce the long-term health care burden for California's public health insurance program.

3. This project directly adds jobs at [REDACTED] and at the California-based companies that are involved in this project.

4. This project will produce intellectual property that is owned by t [REDACTED]. Our team has a track record of attracting out of state private investment to invest in California and of procuring supplies and equipment from strategic California-based companies.

5. This mature project is precisely the type of cutting-edge, multi-disciplinary stem cell project that Californians imagined when they approved proposition 71 in 2004. The establishment of CIRM has transformed the research infrastructure at [REDACTED], increased our ability to recruit world class stem cell scientists, and attracted the attention of superb scientists from other disciplines to this new field. Working together, our team has compiled an impressive list of accomplishments and we are confident in our abilities to take this project to IND submission in a timely fashion. Funding of this project will fulfill the promise of proposition 71.

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